

- 94 -

CLAIMS:

1. A method of eliciting or inducing, in a mammal, an immune response directed to a parasite said method comprising administering to said mammal an effective amount of an immunogenic composition, which composition comprises the inositolglycan domain portion of GPI, which inositolglycan domain portion comprises insufficient lipidic domain to induce or elicit an immune response directed to said lipidic domain.
2. A method according to claim 1 wherein said parasite is *Plasmodium*.
3. A method according to claim 2 wherein said *Plasmodium* is *Plasmodium falciparum*.
4. A method according to claim 3 wherein said GPI molecule is a *Plasmodium falciparum* GPI inositolglycan domain.
5. A method according to claim 4 wherein said GPI inositolglycan domain is synthetically generated.
6. A method according to claim 5 wherein said synthetic GPI inositolglycan domain comprises the structure  
  
EtN-P-(Man $\alpha$ 1,2)-6M $\alpha$ 1, 2M $\alpha$ 1, 6Man $\alpha$ 1, 4GlcNH $_2\alpha$ 1-*myo*-inositol-1,2 cyclic-phosphate  
  
or derivative or equivalent thereof wherein EtN is ethanolamine, P is phosphate and M is mannose.
7. A method according to claim 5 wherein said synthetic GPI inositolglycan domain comprises the structure

- 95 -

$\text{NH}_2\text{-CH}_2\text{-CH}_2\text{-PO}_4\text{-(Man}\alpha\text{1-2) 6Man}\alpha\text{1-2 Man}\alpha\text{1-6Man}\alpha\text{1-4GlcNH}_2\text{-6myo-}$   
 inositol-1,2 cyclic-phosphate

or derivative or equivalent thereof.

8. A method of therapeutically or prophylactically treating a mammal for a parasite infection said method comprising administering to said mammal an effective amount of an immunogenic composition which composition comprises the inositolglycan domain portion of GPI, which inositolglycan domain portion comprises insufficient lipidic domain to induce or elicit an immune response directed to a GPI lipidic domain.
9. A method according to claim 8 wherein said parasite is *Plasmodium*.
10. A method according to claim 9 wherein said *Plasmodium* is *Plasmodium falciparum*.
11. A method according to claim 10 wherein said GPI molecule is a *Plasmodium falciparum* GPI inositolglycan domain.
12. A method according to claim 11 wherein said GPI inositolglycan domain is synthetically generated.
13. A method according to claim 12 wherein said GPI inositolglycan domain comprises the structure

$\text{EtN-P-(Man}\alpha\text{1,2)-6M}\alpha\text{1, 2M}\alpha\text{1, 6Man}\alpha\text{1, 4GlcNH}_2\alpha\text{1-myoinositol-1,2 cyclic-}$   
 phosphate

- 96 -

or derivative or equivalent thereof wherein EtN is ethanolamine, P is phosphate and M is mannose.

14. A method according to claim 12 wherein said GPI inositolglycan domain comprises the structure

$\text{NH}_2\text{-CH}_2\text{-CH}_2\text{-PO}_4\text{-(Man}\alpha\text{1-2) 6Man}\alpha\text{1-2 Man}\alpha\text{1-6Man}\alpha\text{1-4GlcNH}_2\text{-6}myo\text{-inositol-1,2 cyclic-phosphate}$

or derivative or equivalent thereof.

15. A method for the treatment and/or prophylaxis of a mammalian disease condition characterised by a parasite infection, said method comprising administering to said mammal an effective amount of an immunogenic composition which composition comprises the inositolglycan domain portion of GPI, which inositolglycan domain portion comprises insufficient lipidic domain to induce or elicit an immune response directed to said lipidic domain.
16. A method according to claim 15 wherein said parasite is *Plasmodium*.
17. A method according to claim 16 wherein said *Plasmodium* is *Plasmodium falciparum*.
18. A method according to claim 17 wherein said GPI molecule is a *Plasmodium falciparum* GPI inositolglycan domain.
19. A method according to claim 18 wherein said GPI inositolglycan domain is synthetically generated.
20. A method according to claim 19 wherein said GPI inositolglycan domain comprises the structure

- 97 -

EtN-P-(Man $\alpha$ 1,2)-6M $\alpha$ 1, 2M $\alpha$ 1, 6Man $\alpha$ 1, 4GlcNH $\alpha$ 1-*myo*-inositol-1,2 cyclic-phosphate

or derivative or equivalent thereof wherein EtN is ethanolamine, P is phosphate and M is mannose.

21. A method according to claim 19 wherein said GPI inositolglycan domain comprises the structure

NH $_2$ -CH $_2$ -CH $_2$ -PO $_4$ -(Man $\alpha$ 1-2) 6Man $\alpha$ 1-2 Man $\alpha$ 1-6Man $\alpha$ 1-4GlcNH $_2$ -6*myo*-inositol-1,2 cyclic-phosphate

or derivative or equivalent thereof.

22. A method according to any one of claims 15-21 wherein said disease condition is malaria.
23. Use of a composition comprising a parasite GPI inositolglycan domain portion, but which portion is substantially incapable of inducing an immune response directed to a lipidic domain of GPI, in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of a mammalian disease condition characterised by infection with said parasite.
24. Use according to claim 23 wherein said parasite is *Plasmodium*.
25. Use according to claim 24 wherein said GPI inositolglycan domain is synthetically generated.
26. Use according to claim 25 wherein synthetic GPI inositolglycan domain comprises the structure

- 98 -

EtN-P-(Man $\alpha$ 1,2)-6M $\alpha$ 1, 2M $\alpha$ 1, 6Man $\alpha$ 1, 4GlcNH $_2\alpha$ 1-*myo*-inositol-1,2 cyclic-phosphate

or derivative or equivalent thereof wherein EtN is ethanolamine, P is phosphate and M is mannose.

27. Use according to claim 25 wherein said synthetic GPI inositolglycan domain comprises the structure

NH $_2$ -CH $_2$ -CH $_2$ -PO $_4$ -(Man $\alpha$ 1-2) 6Man $\alpha$ 1-2 Man $\alpha$ 1-6Man $\alpha$ 1-4GlcNH $_2$ -6*myo*-inositol-1,2 cyclic-phosphate

or derivative or equivalent thereof.

28. A composition capable of inducing an immune response directed to a parasite said composition comprising a parasite GPI inositolglycan domain portion but which portion is substantially incapable of inducing an immune response to a lipidic domain of a GPI.
29. A composition according to claim 28 wherein said parasite is *Plasmodium*.
30. A composition according to claim 29 wherein said GPI inositolglycan domain is synthetically generated.
31. A composition according to claim 30 wherein said synthetic GPI inositolglycan domain comprises the structure

EtN-P-(Man $\alpha$ 1,2)-6M $\alpha$ 1, 2M $\alpha$ 1, 6Man $\alpha$ 1, 4GlcNH $_2\alpha$ 1-*myo*-inositol-1,2 cyclic-phosphate

- 99 -

or derivative or equivalent thereof wherein EtN is ethanolamine, P is phosphate and M is mannose.

32. A composition according to claim 31 wherein said GPI inositolglycan domain comprises the structure

$\text{NH}_2\text{-CH}_2\text{-CH}_2\text{-PO}_4\text{-(Man}\alpha\text{1-2) 6Man}\alpha\text{1-2 Man}\alpha\text{1-6Man}\alpha\text{1-4GlcNH}_2\text{-6myo-}$   
inositol-1,2 cyclic-phosphate

or derivative or equivalent thereof.

33. A vaccine composition for inducing an immune response to a parasite, said composition comprising as the active component the parasite inositolglycan domain portion of GPI, which inositolglycan portion is substantially incapable of inducing an immune response directed to a lipidic domain of a GPI, together with one or more pharmaceutically acceptable carriers and/or diluents.

34. A vaccine composition according to claim 33 wherein said parasite is *Plasmodium*.

35. A composition according to claim 34 wherein said GPI inositolglycan domain is synthetically generated.

36. A composition according to claim 35 wherein said synthetic GPI inositolglycan domain comprises the structure

$\text{EtN-P-(Man}\alpha\text{1,2)-6M}\alpha\text{1, 2M}\alpha\text{1, 6Man}\alpha\text{1, 4GlcNH}_2\alpha\text{1-my-}$   
inositol-1,2 cyclic-phosphate

or derivative or equivalent thereof wherein EtN is ethanolamine, P is phosphate and M is mannose.

- 100 -

37. A composition according to claim 35 wherein said GPI inositolglycan domain comprises the structure

$\text{NH}_2\text{-CH}_2\text{-CH}_2\text{-PO}_4\text{-(Man}\alpha\text{1-2) 6Man}\alpha\text{1-2 Man}\alpha\text{1-6Man}\alpha\text{1-4GlcNH}_2\text{-6myo-}$   
inositol-1,2 cyclic-phosphate

or derivative or equivalent thereof.

38. A pharmaceutical composition comprising a parasite GPI inositolglycan domain portion but which portion is substantially incapable of inducing an immune response directed to a lipidic domain of a GPI together with one or more pharmaceutically acceptable carriers and/or diluents.

39. A pharmaceutical composition according to claim 38 wherein said parasite is *Plasmodium*.

40. A composition according to claim 39 wherein said GPI inositolglycan domain is synthetically generated.

41. A composition according to claim 40 wherein said synthetic GPI inositolglycan domain comprises the structure

$\text{EtN-P-(Man}\alpha\text{1,2)-6M}\alpha\text{1, 2M}\alpha\text{1, 6Man}\alpha\text{1, 4GlcNH}_2\alpha\text{1-myoinositol-1,2 cyclic-}$   
phosphate

or derivative or equivalent thereof wherein EtN is ethanolamine, P is phosphate and M is mannose.

42. A composition according to claim 41 wherein said GPI inositolglycan domain comprises the structure

- 101 -

$\text{NH}_2\text{-CH}_2\text{-CH}_2\text{-PO}_4\text{-(Man}\alpha\text{1-2) 6Man}\alpha\text{1-2 Man}\alpha\text{1-6Man}\alpha\text{1-4GlcNH}_2\text{-6myo-}$   
 inositol-1,2 cyclic-phosphate

or derivative or equivalent thereof.

43. An antibody directed to a synthetic GPI inositolglycan domain but which antibody is substantially incapable of interacting with the lipidic domain of a GPI.

44. The antibody according to claim 43 wherein said GPI inositolglycan domain comprises the structure

$\text{EtN-P-(Man}\alpha\text{1,2)-6M}\alpha\text{1, 2M}\alpha\text{1, 6Man}\alpha\text{1, 4GlcNH}_2\alpha\text{1-my-}$   
 inositol-1,2 cyclic-phosphate

or derivative or equivalent thereof wherein EtN is ethanolamine, P is phosphate and M is mannose.

45. The antibody according to claim 43 wherein said GPI inositolglycan domain comprises the structure

$\text{NH}_2\text{-CH}_2\text{-CH}_2\text{-PO}_4\text{-(Man}\alpha\text{1-2) 6Man}\alpha\text{1-2 Man}\alpha\text{1-6Man}\alpha\text{1-4GlcNH}_2\text{-6myo-}$   
 inositol-1,2 cyclic-phosphate

or derivative or equivalent thereof.

46. A pharmaceutical composition comprising the antibody of any one of claims 43-45.
47. A method of inhibiting, halting or delaying the onset or progression of a mammalian disease condition characterised by a parasite infection said method comprising administering to said mammal an effective amount of an antibody as claimed in any one of claims 43-45.



- 102 -

48. Use of an antibody according to any one of claims 42-45 in the manufacture of a medicament for inhibiting, halting or delaying the onset or progression of a disease condition characterised by the infection of a mammal by a parasite.
49. A method for detecting, in a biological sample, an immunointeractive molecule directed to a microorganism said method comprising contacting said biological sample with a molecule comprising said microorganism GPI inositolglycan domain or a derivative or equivalent thereof and qualitatively and/or quantitatively screening for said GPI inositolglycan domain-immunointeractive molecule complex formation.
50. A method for detecting, monitoring or otherwise assessing an immune response directed to a microorganism in a subject said method comprising contacting a biological sample, from said subject, with a molecule comprising said microorganism GPI inositolglycan domain-immunointeractive molecule complex formation.
51. The method according to claim 49 or 50 wherein said molecule is a modified GPI molecule or derivative or equivalent thereof and which modified GPI molecule comprises insufficient lipidic domain to induce or elicit an immune response directed to a GPI lipidic domain.
52. The method according to claim 51 wherein said modified GPI molecule is the inositolglycan domain portion of GPI or derivative or equivalent thereof.
53. The method according to claim 51 or 52 wherein said modified GPI molecule is a modified parasite GPI molecule or derivative or equivalent thereof.
54. The method according to claim 53 wherein said parasite is *Plasmodium*.

- 103 -

55. The method according to claim 54 wherein said *Plasmodium* is *Plasmodium falciparum*.
56. The method according to claim 55 wherein said modified *Plasmodium falciparum* GPI molecule is a *Plasmodium falciparum* GPI inositolglycan domain.
57. The method according to claim 56 wherein said GPI inositol glycan domain comprises the structure

ethanolamine-phosphate-(Man $\alpha$ 1,2)-Man $\alpha$ 1,2Man $\alpha$ 1,6Man $\alpha$ 1,4GlcN-*myo*-inositol phosphoglycerol

or derivative or equivalent thereof.

58. The method according to claim 56 wherein said GPI inositol glycan domain comprises the structure

X1 - X2 - X3 -X4 - ethanolamine-phosphate-(Man $\alpha$ 1,2)-  
Man $\alpha$ 1,2Man $\alpha$ 1,6Man $\alpha$ 1,4GlcN-*myo*-inositol phosphoglycerol

wherein X1, X2, X3 and X4 are any 4 amino acids, or derivative or equivalent of said GPI inositolglycan domain.

59. The method according to claim 56 wherein said GPI inositolglycan domain comprises a structure selected from:

EtN-P-[M $\alpha$ 2]M $\alpha$ 2 M $\alpha$ 6 M $\alpha$ 4G $\alpha$ 6Ino  
EtN-P-[M $\alpha$ 2][G]M $\alpha$ 2 M $\alpha$ 6 M $\alpha$ 4G $\alpha$ 6Ino  
EtN-P-[M $\alpha$ 2][X]M $\alpha$ 2 M $\alpha$ 6 M $\alpha$ 4G $\alpha$ 6Ino  
EtN-P-[M $\alpha$ 2][EtN-P]M $\alpha$ 2 M $\alpha$ 6 M $\alpha$ 4G $\alpha$ 6Ino  
EtN-P-M $\alpha$ 2 M $\alpha$ 6 M $\alpha$ 4G

- 104 -

Mo<sub>2</sub> Mo<sub>6</sub> Mo<sub>4</sub>G  
 EtN-P-Mo<sub>2</sub> Mo<sub>6</sub> M  
 EtN-P-[Mo<sub>2</sub>][G]Mo<sub>2</sub> Mo<sub>6</sub> Mo<sub>4</sub>G  
 EtN-P-[Mo<sub>2</sub>][X]Mo<sub>2</sub> Mo<sub>6</sub> Mo<sub>4</sub>G  
 EtN-P-[Mo<sub>2</sub>][EtN-P]Mo<sub>2</sub> Mo<sub>6</sub> Mo<sub>4</sub>G  
 Mo<sub>2</sub> [Mo<sub>2</sub>][G]Mo<sub>2</sub> Mo<sub>6</sub> Mo<sub>4</sub>G  
 Mo<sub>2</sub> [Mo<sub>2</sub>][X]Mo<sub>2</sub> Mo<sub>6</sub> Mo<sub>4</sub>G  
 Mo<sub>2</sub> [Mo<sub>2</sub>][EtN-P]Mo<sub>2</sub> Mo<sub>6</sub> Mo<sub>4</sub>G  
 Mo<sub>6</sub> Mo<sub>4</sub>Gα<sub>6</sub>Ino  
 Mo<sub>2</sub> Mo<sub>6</sub> Mo<sub>4</sub>Gα<sub>6</sub>Ino  
 Mo<sub>2</sub> [Mo<sub>2</sub>]Mo<sub>6</sub> Mo<sub>4</sub>Gα<sub>6</sub>Ino  
 Mo<sub>2</sub> [Mo<sub>2</sub>][G]Mo<sub>6</sub> Mo<sub>4</sub>Gα<sub>6</sub>Ino  
 Mo<sub>2</sub> [Mo<sub>2</sub>][X]Mo<sub>6</sub> Mo<sub>4</sub>Gα<sub>6</sub>Ino  
 EtN-P-[Mo<sub>2</sub>][G]Mo<sub>2</sub> Mo<sub>6</sub> M  
 EtN-P-[Mo<sub>2</sub>][X]Mo<sub>2</sub> Mo<sub>6</sub> M  
 EtN-P-[Mo<sub>2</sub>][EtN-P]Mo<sub>2</sub> Mo<sub>6</sub> M  
 Mo<sub>2</sub> [Mo<sub>2</sub>][G]Mo<sub>2</sub> Mo<sub>6</sub> M  
 Mo<sub>2</sub> [Mo<sub>2</sub>][X]Mo<sub>2</sub> Mo<sub>6</sub> M  
 Mo<sub>2</sub> [Mo<sub>2</sub>][EtN-P]Mo<sub>2</sub> Mo<sub>6</sub> M  
 Mo<sub>2</sub> Mo<sub>6</sub> M  
 Mo<sub>6</sub> Mo<sub>4</sub>G  
 EtN-P-[Mo<sub>2</sub>][G]Mo<sub>2</sub> M  
 EtN-P-[Mo<sub>2</sub>][X]Mo<sub>2</sub> M  
 EtN-P-[Mo<sub>2</sub>][EtN-P]Mo<sub>2</sub> M

or derivative or equivalent thereof wherein EtN is ethanolamine, P is phosphate, M is mannose, G is non-N-acetylated glucosamine, [G] is any non-N-acetylated hexosamine, Ino is inositol or inositol-phosphoglycerol, [X] is any other substituent, α represents α-linkages which may be substituted with β-linkages wherever required, and numeric values represent positional linkages which may be substituted with any other positional linkages as required.

- 105 -

60. The method according to claim 56 wherein said GPI inositolglycan domain is synthetically generated.

61. The method according to claim 60 wherein said synthetic GPI inositolglycan domain comprises the structure

EtN-P-(Man $\alpha$ 1,2)-6M $\alpha$ 1, 2M $\alpha$ 1, 6Man $\alpha$ 1, 4GlcNH $_2\alpha$ 1-*myo*-inositol-1,2 cyclic-phosphate

or derivative or equivalent thereof wherein EtN is ethanolamine, P is phosphate and M is mannose.

62. The method according to claim 61 wherein said synthetic GPI inositolglycan domain comprises the structure

NH $_2$ -CH $_2$ -CH $_2$ -PO $_4$ -(Man $\alpha$ 1-2) 6Man $\alpha$ 1-2 Man $\alpha$ 1-6Man $\alpha$ 1-4GlcNH $_2$ -6*myo*-inositol-1,2 cyclic-phosphate

or derivative or equivalent thereof.

63. A modular kit comprising one or members wherein at least one member is a solid support comprising a GPI molecule as defined in any one of claims 48-61.

64. A method for analysing, designing and/or modifying an agent capable of interacting with an anti-GPI glycan immunointeractive molecule binding site, which immunointeractive molecule is identifiable utilising the diagnostic methodology defined in accordance with any one of claims 48-61 said method comprising contacting said immunointeractive molecule or derivative thereof with a putative agents and assessing the degree of interactive complementarity of said agent with said binding site.

- 106 -

65. The use of the agent developed in accordance with the method of claim 64 in the method of any one of claims 1-22 or 47-62, the composition of any one of claims 28-42 or the use of any one of claims 23-27.